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kknezek@sidley.com

March 14, 2002

Box PCT
Assistant Director For Patents
Washington, D.C. 20231

Re: National Phase Entry in the United States of
PCT Application No. PCT/US00/26438
International Filing Date: September 26, 2000
Priority Date: September 28, 1999
For: THROMBOTIC EPISODE RISK ASSAYS USING
OXIDIZED PHOSPHOLIPIDS
By: Naomi L. ESMON et al.
Attorney Docket No. 11146/10904

EXPRESS MAIL MAILING LABEL NO.: EL 861131911 US
DATE OF DEPOSIT: MARCH 14, 2002

I hereby certify that this paper or fee is being deposited
with the United States Postal Service "Express Mail Post
Office to Addressee" service under 37 C.F.R. § 1.10 on the
dated indicated above and is addressed to:
BOX PCT, Assistant Director for Patents, Washington,
DC 20231.

Derrick Gordon

Name of Person Mailing Paper or Fee

Derrick Gordon

Signature

MARCH 14, 2002

Date of Signature

Dear Sir:

Enclosed for filing in connection with national phase entry in the United States of PCT patent
application PCT/US00/26438 is Form PTO-1390 (Transmittal Letter to the United States Designated/Elected
Office (DO/EO/US) Concerning a Filing Under 35 U.S.C. 371) and a Preliminary Amendment.

Sincerely,

Karen L. Knezek

Karen L. Knezek
Registration No. 39,253
Agent for Applicants

KLK/fis
Enclosures

PATEI COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE
 in its capacity as elected Office

Date of mailing (day/month/year) 12 June 2001 (12.06.01)	
International application No. PCT/US00/26438	Applicant's or agent's file reference 11146/10902
International filing date (day/month/year) 26 September 2000 (26.09.00)	Priority date (day/month/year) 28 September 1999 (28.09.99)
Applicant ESMON, Naomi, L. et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

18 April 2001 (18.04.01)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer P. Blanchet (Fax 338.87.40) Telephone No.: (41-22) 338.83.38
--	--

PATENT COOPERATION TREATY

PCT

From the INTERNATIONAL BUREAU

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

To:

HANSEN, Eugenia, S.
Sidley Austin Brown & Wood
Suite 3400
717 North Harwood
Dallas, TX 75201
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 07 November 2001 (07.11.01)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference 11146/10902	
International application No. PCT/US00/26438	International filing date (day/month/year) 26 September 2000 (26.09.00)

1. The following indications appeared on record concerning:

☐ the applicant ☐ the inventor ☒ the agent ☐ the common representative

Name and Address HANSEN, Eugenia, S. Sidley & Austin Suite 3400 717 N. Harwood Dallas, TX 75201 United States of America	State of Nationality	State of Residence
	Telephone No. 214-981-3315	
	Facsimile No. 214-981-3400	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person ☐ the name ☒ the address ☐ the nationality ☐ the residence

Name and Address HANSEN, Eugenia, S. Sidley Austin Brown & Wood Suite 3400 717 North Harwood Dallas, TX 75201 United States of America	State of Nationality	State of Residence
	Telephone No. 214-981-3315	
	Facsimile No. 214-981-3400	
	Teleprinter No.	

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned
<input checked="" type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Idhir BRITEL
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 11146/10902	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/26438	International filing date (day/month/year) 26/09/2000	Priority date (day/month/year) 28/09/1999
International Patent Classification (IPC) or national classification and IPC G01N33/92		
Applicant OKLAHOMA MEDICAL RESEARCH FOUNDATION et al.		



1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.

- ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 4 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 18/04/2001	Date of completion of this report 11.01.2002
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Linker, W Telephone No. +49 89 2399 8703 

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/26438

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*):

Description, pages:

1-15 as originally filed

Claims, No.:

1-29 as received on 29/10/2001 with letter of 29/10/2001

Drawings, sheets:

1/1 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/26438

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims 3-29
	No: Claims 1, 2
Inventive step (IS)	Yes: Claims
	No: Claims 1-29
Industrial applicability (IA)	Yes: Claims 1-29
	No: Claims

2. Citations and explanations
see separate sheet

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

- D1: AVIRAM M ET AL: 'OXIDIZED LOW-DENSITY LIPOPROTEIN REDUCES PLASMA COAGULATION IN-VITRO' SCANDINAVIAN JOURNAL OF CLINICAL AND LABORATORY INVESTIGATION, vol. 51, no. 1, 1991, pages 17-22, XP000991385 ISSN: 0036-5513
- D2: US-A-5 472 852 (SMIRNOV MIKHAIL D ET AL) 5 December 1995 (1995-12-05) cited in the application
- D3: BARROWCLIFFE T W ET AL: 'PHOSPHO LIPID REAGENTS USED IN COAGULATION 2. FACTORS INFLUENCING THEIR SENSITIVITY TO HEPARIN' THROMBOSIS AND HAEMOSTASIS, vol. 46, no. 3, 1981, pages 634-637, XP000991386 ISSN: 0340-6245
- D4: BARROWCLIFFE T W ET AL: 'PHOSPHO LIPID REAGENTS USED IN COAGULATION 1. SOME GENERAL PROPERTIES AND THEIR SENSITIVITY TO FACTOR-VIII' THROMBOSIS AND HAEMOSTASIS, vol. 46, no. 3, 1981, pages 629-633, XP000991384 ISSN: 0340-6245
- D5: HORKKO SOHVI ET AL: 'Antiphospholipid antibodies are directed against epitopes of oxidized phospholipids: Recognition of cardiolipin by monoclonal antibodies to epitopes of oxidized low density lipoprotein.' JOURNAL OF CLINICAL INVESTIGATION, vol. 98, no. 3, 1996, pages 815-825, XP002163435 ISSN: 0021-9738 cited in the application

While the applicant's observations submitted with the amended claims have been considered, the previously expressed opinion is nevertheless maintained for the following reasons:

Documents D3 and D4 disclose likewise a set of reagents of oxidised and non-oxidised phospholipid reagent, see D3, Table 5 or D4 Table 4. Both documents are therefore considered to be still detrimental to the novelty and inventive step of claim 2 (Article 33(2) and (3) PCT).

Document D1 discloses a coagulation assay using LDL and Ox-LDL, see page 17 under "Materials and Methods". In view of the fact that LDL per se also contains phospholipids, the present wording of claims 1 and 2 encompass method and reagents known from D1. Therefore, D1 is still considered to be detrimental to novelty and inventive step of claims 1 and 2 (Article 33(2) and (3) PCT).

Document D5 discloses that antiphospholipid autoantibodies are directed to epitopes of oxidised phospholipids, see page 816, right column under "Determination of autoantibody titers against oxidised LDL". Document D2 discloses an assay for detecting the propensity of patients having autoantibodies. As all measures indicated in claims 3-29 appear to be derivable from documents D2 and D5, these claims are therefore considered to lack an inventive step under Article 33(3) PCT.

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
5 April 2001 (05.04.2001)

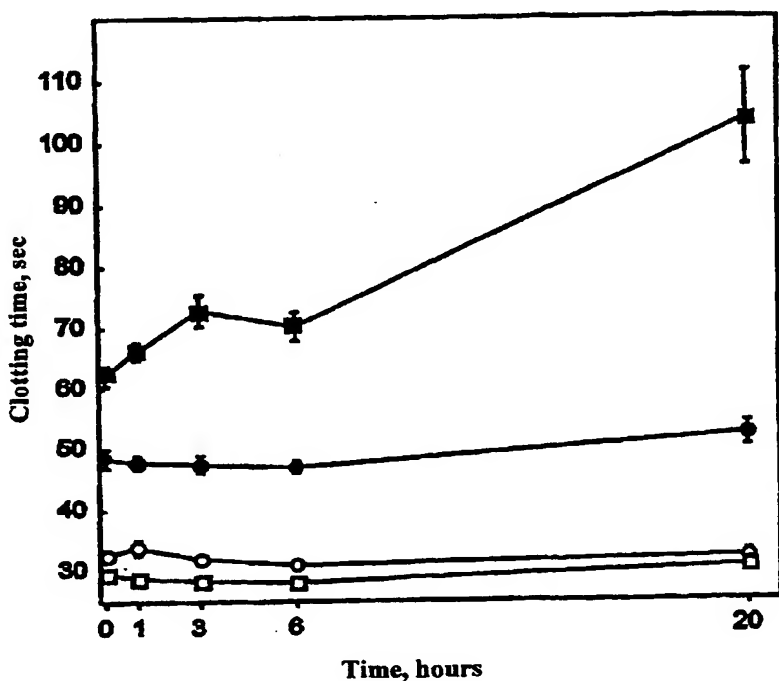
PCT

(10) International Publication Number
WO 01/23895 A3

- (51) International Patent Classification⁷: G01N 33/86
- (21) International Application Number: PCT/US00/26438
- (22) International Filing Date:
26 September 2000 (26.09.2000)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/156,564 28 September 1999 (28.09.1999) US
- (71) Applicant (for all designated States except US): OKLAHOMA MEDICAL RESEARCH FOUNDATION [US/US]; 825 N.E. 13th Street, Oklahoma City, OK 73104 (US).
- (72) Inventors; and
(75) Inventors/Applicants (for US only): ESMON, Naomi, L. [US/US]; 5800 North Stonewall Drive, Oklahoma City, OK 73111 (US). SAFA JAMILABADI, Omid [IR/US]; 13321 Plaza Terrace, #285, Oklahoma City, OK 73120 (US).
- (74) Agents: HANSEN, Eugenia, S. et al.; Sidley & Austin, Suite 3400, 717 N. Harwood, Dallas, TX 75201 (US).
- (81) Designated States (national): AU, CA, JP, US.
- (84) Designated States (regional): European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).
- Published:**
- With international search report.
 - Before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments.

[Continued on next page]

(54) Title: THROMBOTIC EPISODE RISK ASSAYS USING OXIDIZED PHOSPHOLIPIDS



(57) Abstract: An assay to assess thrombotic risk in which oxidized lipids comprising phospholipids are utilized as a membrane source in a clotting assay and the results compared to an assay in which unoxidized phospholipid is used as a membrane source in the presence and absence of activated protein C ("APC"). The assay can monitor for the presence of antibodies in the patient which interfere specifically with the anticoagulant function of APC in an oxidation dependent or independent manner. This can indicate the propensity of the patient to experience episodes of vein thrombosis or arterial thrombosis.

- PE:PS:PC + APC
- PS:PC + APC
- PS:PC
- PE:PS:PC

WO 01/23895 A3



(88) Date of publication of the international search report:
7 June 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

Inventor's Application No.

PCT/US 00/26438

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/86

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	AVIRAM M ET AL: "OXIDIZED LOW-DENSITY LIPOPROTEIN REDUCES PLASMA COAGULATION IN-VITRO" SCANDINAVIAN JOURNAL OF CLINICAL AND LABORATORY INVESTIGATION, vol. 51, no. 1, 1991, pages 17-22, XP000991385 ISSN: 0036-5513	1-6
Y	the whole document --- -/--	1,7-29

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *Z* document member of the same patent family

Date of the actual completion of the international search

20 March 2001

Date of mailing of the international search report

02/04/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Hart-Davis, J

INTERNATIONAL SEARCH REPORT

In. ation Application No

PCT/US 00/26438

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication where appropriate, of the relevant passages	Relevant to claim No.
X	<p>BARROWCLIFFE T W ET AL: "PHOSPHO LIPID REAGENTS USED IN COAGULATION 2. FACTORS INFLUENCING THEIR SENSITIVITY TO HEPARIN" THROMBOSIS AND HAEMOSTASIS, vol. 46, no. 3, 1981, pages 634-637, XP000991386 ISSN: 0340-6245 page 636, column 1, paragraph 1 page 637; table 1</p> <p style="text-align: center;">---</p>	2-6
X	<p>BARROWCLIFFE T W ET AL: "PHOSPHO LIPID REAGENTS USED IN COAGULATION 1. SOME GENERAL PROPERTIES AND THEIR SENSITIVITY TO FACTOR-VIII" THROMBOSIS AND HAEMOSTASIS, vol. 46, no. 3, 1981, pages 629-633, XP000991384 ISSN: 0340-6245 page 631, column 2, paragraph 2 page 632, column 1, paragraph 3</p> <p style="text-align: center;">---</p>	2-6
Y	<p>US 5 472 852 A (SMIRNOV MIKHAIL D ET AL) 5 December 1995 (1995-12-05) cited in the application the whole document</p> <p style="text-align: center;">---</p>	1,7-29
A	<p>JAIN S K: "IN-VIVO EXTERNALIZATION OF PHOSPHATIDYLSERINE AND PHOSPHATIDYLETHANOLAMINE IN THE MEMBRANE BILAYER AND HYPERCOAGULABILITY BY THE LIPID PEROXIDATION OF ERYTHROCYTES IN RATS" JOURNAL OF CLINICAL INVESTIGATION, vol. 76, no. 1, 1985, pages 281-286, XP000991383 ISSN: 0021-9738 the whole document</p> <p style="text-align: center;">---</p>	1,7,13
A	<p>LESNIK PHILIPPE ET AL: "Tissue Factor Pathway Inhibitor Activity Associated With LDL Is Inactivated by Cell- and Copper-Mediated Oxidation." ARTERIOSCLEROSIS THROMBOSIS AND VASCULAR BIOLOGY, vol. 15, no. 8, 1995, pages 1121-1130, XP000991388 ISSN: 1079-5642 the whole document</p> <p style="text-align: center;">---</p>	1,7,13
	-/--	

INTERNATIONAL SEARCH REPORT

In ation Application No

PCT/US 00/26438

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	SMIRNOV MICHAEL D ET AL: "The effect of membrane composition on the hemostatic balance." BIOCHEMISTRY, vol. 38, no. 12, 23 March 1999 (1999-03-23), pages 3591-3598, XP002163434 ISSN: 0006-2960 cited in the application the whole document ----	
A	HORKKO SOHVI ET AL: "Antiphospholipid antibodies are directed against epitopes of oxidized phospholipids: Recognition of cardiolipin by monoclonal antibodies to epitopes of oxidized low density lipoprotein." JOURNAL OF CLINICAL INVESTIGATION, vol. 98, no. 3, 1996, pages 815-825, XP002163435 ISSN: 0021-9738 cited in the application the whole document ----	
P,A	ESMON NAOMI L ET AL: "Antiphospholipid antibodies and the protein C pathway." JOURNAL OF AUTOIMMUNITY, vol. 15, no. 2, 2000, pages 221-225, XP000992142 ISSN: 0896-8411 page 223 -----	

INTERNATIONAL SEARCH REPORT

Information on patent family members

In .ation Application No

PCT/US 00/26438

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5472852 A	05-12-1995	AU 695553 B	13-08-1998
		AU 7729394 A	03-04-1995
		CA 2171721 A	23-03-1995
		DE 69403088 D	12-06-1997
		DE 69403088 T	18-12-1997
		EP 0719415 A	03-07-1996
		WO 9508121 A	23-03-1995
<hr/>			

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 11146/10902	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 00/ 26438	International filing date (day/month/year) 26/09/2000	(Earliest) Priority Date (day/month/year) 28/09/1999
Applicant OKLAHOMA MEDICAL RESEARCH FOUNDATION et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.



as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.

1



None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PC 00/26438

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N33/86

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	AVIRAM M ET AL: "OXIDIZED LOW-DENSITY LIPOPROTEIN REDUCES PLASMA COAGULATION IN-VITRO" SCANDINAVIAN JOURNAL OF CLINICAL AND LABORATORY INVESTIGATION, vol. 51, no. 1, 1991, pages 17-22, XP000991385	1-6
Y	ISSN: 0036-5513 the whole document --- -/--	1,7-29

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
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- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- * & * document member of the same patent family

Date of the actual completion of the international search

20 March 2001

Date of mailing of the international search report

02/04/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Hart-Davis, J

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>BARROWCLIFFE T W ET AL: "PHOSPHO LIPID REAGENTS USED IN COAGULATION 2. FACTORS INFLUENCING THEIR SENSITIVITY TO HEPARIN" THROMBOSIS AND HAEMOSTASIS, vol. 46, no. 3, 1981, pages 634-637, XP000991386 ISSN: 0340-6245 page 636, column 1, paragraph 1 page 637; table 1</p> <p>---</p>	2-6
X	<p>BARROWCLIFFE T W ET AL: "PHOSPHO LIPID REAGENTS USED IN COAGULATION 1. SOME GENERAL PROPERTIES AND THEIR SENSITIVITY TO FACTOR-VIII" THROMBOSIS AND HAEMOSTASIS, vol. 46, no. 3, 1981, pages 629-633, XP000991384 ISSN: 0340-6245 page 631, column 2, paragraph 2 page 632, column 1, paragraph 3</p> <p>---</p>	2-6
Y	<p>US 5 472 852 A (SMIRNOV MIKHAIL D ET AL) 5 December 1995 (1995-12-05) cited in the application the whole document</p> <p>---</p>	1,7-29
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